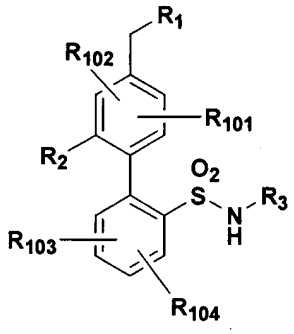
AMENDMENT

In the claims:

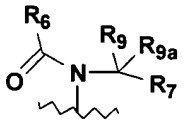
Please amend claim 1 as follows:

1. (Currently Amended) A compound of the following formula I, enantiomers, diastereomers, salts and solvates thereof:



I

wherein:



R_1 is D ;

R_2 is hydrogen, halogen, -CHO, alkyl, haloalkyl, (cycloalkyl)alkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkoxyalkyl, alkoxy, aryloxy alkoxyalkoxy, cyano, hydroxy, hydroxyalkyl, nitro, $-CH(OR_{13})(OR_{14})$, or $-(CH_2)_wY[[;]]$, wherein said (cylcoalkyl) may be optionally substituted by one or more hydrogen, halogen, cyano, alkyl, hydroxyalkyl, alkoxy, nitro or trifluoromethyl groups;

R_3 is heteroaryl[[;]],which may be optionally substituted by one or more hydrogen, halogen, cyano, alkyl, hydroxyalkyl, alkoxy, nitro or trifluoromethyl groups;

R_6 is alkyl, hydroxyalkyl, haloalkyl, hydroxy substituted haloalkyl, cycloalkyl, hydroxy substituted cycloalkyl, (cycloalkyl)alkyl, hydroxy substituted (cycloalkyl)alkyl, aralkyl, alkoxy, hydroxy substituted alkoxy, alkoxyalkyl, hydroxy substituted alkoxyalkyl, or $-NR_{16}R_{17}[[;]]$, wherein said cycloalkyl or (cylcoalkyl) may be

optionally substituted by one or more hydrogen, halogen, cyano, alkyl, hydroxyalkyl, alkoxy, nitro or trifluoromethyl groups;

R_7 is $-(CH_2)_w-CO_2R_{15}$, $-(CH_2)_w-(C=O)NR_{16}R_{17}$, $-(CH_2)_w-NR_{15}(C=O)NR_{16}R_{17}$, $-(CH_2)_w-CH_2OH$, $-(CH_2)_w-(C=O)R_{15}$, tetrazolyl, oxadiazolyl or triazolyl wherein said tetrazolyl, oxadiazolyl or triazolyl may optionally be substituted with hydrogen, alkyl, hydroxy or halogen;

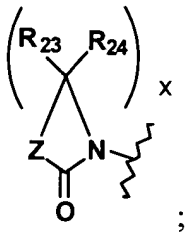
R_9 and R_{9a} are each independently hydrogen, halogen, alkyl, hydroxyalkyl, cycloalkyl, (cycloalkyl)alkyl, aryl, heteroaryl, arylalkyl, alkylthioalkyl, alkoxy or alkoxyalkyl, or R_9 and R_{9a} together with the carbon atom to which they are bonded form a cycloalkyl ring[[;]], wherein each of said cycloalkyl, (cylcoalkyl), aryl alone or as part of another group, heteroaryl, and cycloalkyl ring may be optionally substituted by one or more hydrogen, halogen, cyano, alkyl, hydroxyalkyl, alkoxy, nitro or trifluoromethyl groups;

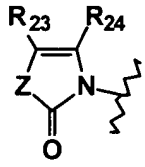
R_{13} and R_{14} are alkyl or together form a five to six-membered cycloalkyl ring[[;]], which may be optionally substituted by one or more hydrogen, halogen, cyano, alkyl, hydroxyalkyl, alkoxy, nitro or trifluoromethyl groups;

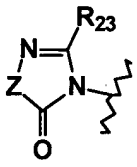
R_{15}, R_{16} and R_{17} are independently hydrogen, alkyl, hydroxyalkyl, cycloalkyl, (cycloalkyl)alkyl, alkoxyalkyl, aralkyl, heterocycloalkyl, aryl, heteroaryl or $-(CH_2)_wQ$, or R_{16} and R_{17} may together form a four to six–membered heterocyclic ring[[;]], wherein each of said cycloalkyl, (cylcoalkyl), aryl alone or as part of another group, heteroaryl, and heterocyclic ring may be optionally substituted by one or more hydrogen, halogen, cyano, alkyl, hydroxyalkyl, alkoxy, nitro or trifluoromethyl groups;

w is 0, 1, or 2;

Y is heteroaryl, -COOH, $-COOR_{18}$, $-CONR_{19}R_{20}$, $-NR_{19}R_{20}$, $-NR_{19}-OR_{20}$, $-NR_{21}(C=O)R_{22}$, $-NR_{21}(C=O)NR_{19}R_{20}$, $-N(R_{19})-(alk)-NR_{21}(C=O)R_{22}$, $-NR_{21}(C=O)OR_{18}$, $-NR_{21}SO_2R_{22}$, $-SO_2R_{22}$, Q, R or S[[;]], wherein said heteroaryl may be optionally substituted by one or more hydrogen, halogen, cyano, alkyl, hydroxyalkyl, alkoxy, nitro or trifluoromethyl groups;

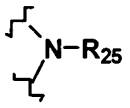
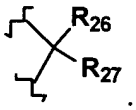
Q is  ;

R is  ;

S is  ;

R_{18}, R_{19}, R_{20}, R_{21} and R_{22} are each independently hydrogen, alkyl, haloalkyl, alkoxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, or R_{19} and R_{20} may together form a four to seven-membered heterocyclic ring[[;]], wherein each of said cycloalkyl, aryl alone or as part of another group, heteroaryl, and heterocyclic ring may be optionally substituted by one or more hydrogen, halogen, cyano, alkyl, hydroxyalkyl, alkoxy, nitro or trifluoromethyl groups;

R_{23} and R_{24} are each independently hydrogen, alkyl or cycloalkyl, or may together form a three to seven membered cycloalkyl ring[[;]], wherein each of said cycloalkyl and cycloalkyl ring may be optionally substituted by one or more hydrogen, halogen, cyano, alkyl, hydroxyalkyl, alkoxy, nitro or trifluoromethyl groups;

Z is oxygen,  or  ;

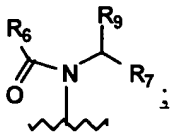
x is 2, 3 or 4;

R_{25}, R_{26} and R_{27} are each independently hydrogen, alkyl or cycloalkyl, or R_{26} and R_{27} may together form a three to seven-membered cycloalkyl ring[[;]], wherein each of said cycloalkyl and cycloalkyl ring may be optionally substituted by one or more hydrogen, halogen, cyano, alkyl, hydroxyalkyl, alkoxy, nitro or trifluoromethyl groups;

R_{101}, R_{102}, R_{103}, and R_{104} are each independently hydrogen, halogen, -CHO, alkyl, haloalkyl, (cycloalkyl)alkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkoxyalkyl, alkoxy, alkoxyalkoxy, cyano, hydroxy, hydroxyalkyl, nitro, $-CH(OR_{13})(OR_{14})$, or $-(CH_2)_wY$[[;]], wherein said (cycloalkyl) may be optionally substituted by one or more hydrogen, halogen, cyano, alkyl, hydroxyalkyl, alkoxy, nitro or trifluoromethyl groups[[;]].

~~wherein said rings; aryl alone or as part of another group; or heteroaryl alone or as part of another group may each optionally be substituted by one or more hydrogen, halogen, cyano, alkyl, hydroxyalkyl, alkoxy, nitro or trifluoromethyl groups.~~

2. (Previously Presented) A compound of claim 1, wherein

R_1 is 

D;

R_2 is hydrogen, alkyl, haloalkyl, (cycloalkyl)alkyl, alkoxyalkyl, haloalkoxyalkyl, alkoxy, alkoxyalkoxy, hydroxyalkyl, or $-(CH_2)_wY$;

R_3 is isoxazolyl pyridizinyl, pyrazinyl or pyrimidinyl, each optionally independently substituted with one to three substituents selected from hydrogen, halogen, cyano, alkyl, alkoxy, trifluoromethyl or nitro;

R_6 is alkyl, haloalkyl, cycloalkyl or alkoxy;

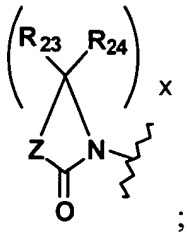
R_7 is $-CO_2R_{15}$, $-(C=O)NR_{16}R_{17}$ or $-CH_2OH$;

R_9 is hydrogen, halogen, alkyl, cycloalkyl, alkoxy or alkoxyalkyl;

R_{15}, R_{16} and R_{17} are independently hydrogen, alkyl or cycloalkyl or R_{16} and R_{17} may together form a four to six–membered heterocyclic ring;

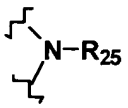
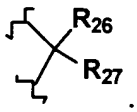
w is 0, 1, or 2;

Y is $-COOR_{18}$, $-NR_{21}(C=O)R_{22}$, $-NR_{21}(C=O)NR_{19}R_{20}$, $-NR_{21}(C=O)OR_{18}$, $-NR_{21}SO_2R_{22}$, $-SO_2R_{22}$ or Q ;

Q is  ;

R_{18}, R_{19}, R_{20}, R_{21} and R_{22} are each independently hydrogen, alkyl, cycloalkyl, or R_{19} and R_{20} may together form a four to seven-membered heterocyclic ring;

R_{23} and R_{24} are each independently hydrogen, alkyl or cycloalkyl, or may together form a three to seven membered cycloalkyl ring;

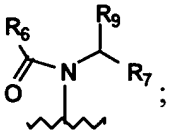
Z is oxygen,  or  ;

x is 2, 3 or 4;

R_{25}, R_{26} and R_{27} are each independently hydrogen, alkyl or cycloalkyl, or R_{26} and R_{27} may together form a three to seven-membered cycloalkyl ring;

R_{101}, R_{102}, R_{103}, and R_{104} are each independently hydrogen, halogen, alkoxy or alkyl.

3. (Previously Presented) A compound of claim 1, wherein

R_1 is  ;

D

R_2 is hydrogen, alkyl, haloalkyl, (cycloalkyl)alkyl, alkoxyalkyl, haloalkoxyalkyl, alkoxy, hydroxyalkyl,or $-(CH_2)_wY$;

R_3 is isoxazolyl, optionally independently substituted with one or two substituents selected from hydrogen, halogen, cyano, alkyl, alkoxy, trifluoromethyl or nitro;

R_6 is alkyl, haloalkyl, cycloalkyl or alkoxy;

R_7 is $-CO_2R_{15}$ or $-(C=O)NR_{16}R_{17}$;

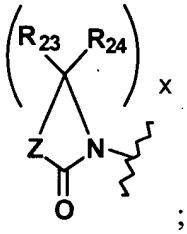
R_9 is hydrogen, halogen, alkyl, cycloalkyl, alkoxy or alkoxyalkyl;

R_{15}, R_{16} and R_{17} are independently hydrogen, alkyl, or cycloalkyl or R_{16} and R_{17} may together form a four to six–membered heterocyclic ring;

n is 2;

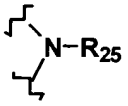
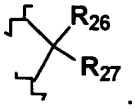
w is 0, 1, or 2;

Y is $-NR_{21}(C=O)R_{22}$, $-NR_{21}(C=O)NR_{19}R_{20}$, $-NR_{21}(C=O)OR_{18}$, $-NR_{21}SO_2R_{22}$, $-SO_2R_{22}$ or Q ;

Q is  ;

R_{18}, R_{19}, R_{20}, R_{21} and R_{22} are each independently hydrogen, alkyl, cycloalkyl, or R_{19} and R_{20} may together form a four to seven-membered heterocyclic ring;

R_{23} and R_{24} are each independently hydrogen, alkyl or cycloalkyl, or may together form a three to seven membered cycloalkyl ring;

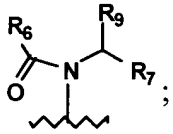
Z is oxygen,  or  ;

x is 2, 3 or 4;

R_{25}, R_{26} and R_{27} are each independently hydrogen, alkyl or cycloalkyl, or R_{26} and R_{27} may together form a three to seven-membered cycloalkyl ring;

R_{101}, R_{102}, R_{103}, and R_{104} are each independently hydrogen, halogen, or alkyl.

4. (Previously Presented) A compound of claim 1, wherein

R_1 is  ;

D

R_2 is hydrogen, alkyl, haloalkyl, (cycloalkyl)alkyl, alkoxyalkyl, haloalkoxyalkyl, alkoxy, alkoxyalkoxy, hydroxyalkyl, or $-(CH_2)_wY$;

R_3 is isoxazol-5-yl or isoxazol-3-yl independently substituted with two substituents selected from alkyl or halogen;

R_6 is alkyl, haloalkyl, cycloalkyl or alkoxy;

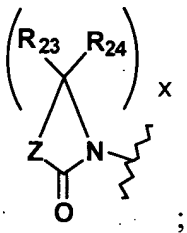
R_7 is $-(C=O)NR_{16}R_{17}$;

R_9 is H, alkyl, cycloalkyl, alkoxy or alkoxyalkyl;

n is 2;

w is 0, 1, or 2;

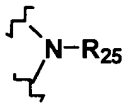
Y is $-NR_{21}(C=O)R_{22}$, $-NR_{21}(C=O)NR_{19}R_{20}$, $-NR_{21}(C=O)OR_{18}$, $-NR_{21}SO_2R_{22}$ or Q ;

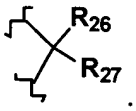
Q is 

;

R_{18}, R_{19}, R_{20}, R_{21} and R_{22} are each independently hydrogen, alkyl, cycloalkyl, or R_{19} and R_{20} may together form a four-, five-, six- or to seven-membered heterocyclic ring;

R_{23} and R_{24} are each independently hydrogen, alkyl or cycloalkyl, or may together form a three to seven membered cycloalkyl ring;

Z is 

or 

;

x is 2;

R_{25}, R_{26} and R_{27} are each independently hydrogen, alkyl or cycloalkyl, or R_{26} and R_{27} may together form a three-, four-, five, six- or seven-membered cycloalkyl ring;

R_{101}, R_{102}, R_{103}, and R_{104} are each independently hydrogen, halogen, or alkyl.

5. (Original) A compound of claim 1, wherein R_3 is isoxazol-5-yl or isoxazol-3-yl independently substituted with two substituents selected from alkyl or halogen.

6-17. (Cancelled)

18. (Previously Presented) A compound of claim 1, wherein R_2 is alkoxyalkyl, haloalkyl or haloalkoxyalkyl.

19. (Original) A compound of claim 18, wherein R_3 is isoxazol-5-yl or isoxazol-3-yl independently substituted with two substituents selected from alkyl or halogen.

20. (Original) A compound of claim 1, wherein R_2 is $-CH_2Y$.

21. (Original) A compound of claim 20, wherein R_3 is isoxazol-5-yl or isoxazol-3-yl independently substituted with two substituents selected from alkyl or halogen.

22. (Original) A compound of claim 20, wherein Y is Q.

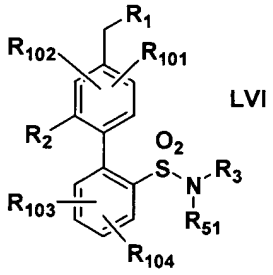
23. (Original) A compound of claim 22, wherein R_3 is isoxazol-5-yl or isoxazol-3-yl independently substituted with two substituents selected from alkyl or halogen.

24-45. (Cancelled)

46. (Original) A pharmaceutical composition for the treatment of an endothelin-dependent or angiotensin II-dependent disorder, comprising a pharmaceutically acceptable vehicle or diluent and at least one compound of claim 1 in an amount effective therefor.

47-48. (Cancelled)

49. (Previously Presented) A compound of the formula



LVI

wherein R_1, R_2, R_3, R_{101}, R_{102}, R_{103}, and R_{104} are as defined in claim 1; and
R_{51} is a suitable nitrogen protecting group.

50. (Original) The compound of claim 49, wherein R_{51} is $-CH_2OCH_2CH_2OCH_3$, $-CH_2OCH_2CH_2Si(CH_3)_3$, $-CH_2OCH_3$, or $-CH_2OCH_2$-aryl.

51-60. (Cancelled)

61. (Original) N2-[[2'-[[(4,5-Dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-methyl-N2-(1-oxobutyl)-L-valinamide or a salt, enantiomer or diasteriomer thereof.

62-68. (Cancelled)

69. (Previously Presented) A compound of claim ~~68~~ 1, wherein R_2 is hydrogen, alkyl, haloalkyl, alkoxyalkyl or haloalkoxyalkyl and R_{101}, R_{102}, R_{103}, R_{104} are each independently hydrogen, halogen, or alkyl.

70. (Previously Presented) A compound of claim 1 wherein R_2 is $-CH_2Y$.

71. (Original) A compound of claim 70, wherein Y is Q.

72-92. (Cancelled)

93. (Original) The pharmaceutical composition of claim 46 further comprising at least one ACE inhibitor.

94. (Original) The pharmaceutical composition of claim 93 wherein said ACE inhibitor is selected from captopril, zofenopril, fosinopril, ceranapril, alacepril, enalapril, delapril, pentopril, quinapril, ramipril, or lisinopril.

95. (Original) The pharmaceutical composition of claim 46 further comprising at least one vasopepsidase inhibitor.

96. (Original) The pharmaceutical composition of claim 95 wherein said vasopepsidase inhibitor is selected from omapatrilat or gemopatrilat.

97. (Original) The pharmaceutical composition of claim 46 further comprising at least one HMG CoA reductase inhibitor.

98. (Original) The pharmaceutical composition of claim 97 wherein said HMG CoA reductase inhibitor is selected from pravastatin, lovastatin, atorvastatin, simvastatin, NK-104 or ZD-4522.

99. (Original) The pharmaceutical composition of claim 46 further comprising at least one anti-platelet agent.

100. (Original) The pharmaceutical composition of claim 99 wherein said anti-platelet agent is selected from clopidigrel, ticlopidine, CS-747 or aspirin.

101. (Original) The pharmaceutical composition of claim 46 further comprising at least one anti-diabetic agent.

102. (Original) The pharmaceutical composition of claim 101 wherein said anti-diabetic agent is selected from biguanides or biguanide/glyburide combinations.

103. (Original) The pharmaceutical composition of claim 46 further comprising at least one beta-adrenergic agent.

104. (Original) The pharmaceutical composition of claim 103 wherein said beta-adrenergic agent is selected from carvedilol or metoprolol.

105. (Original) The pharmaceutical composition of claim 46 further comprising at least one mineralocorticoid receptor antagonist.

106. (Original) The pharmaceutical composition of claim 105 wherein said mineralocorticoid receptor antagonist is selected from spironolactone or eplerenone.

107-108. (Cancelled)